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Petros Tsipouras

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EXAMINER

CLOW, LORI A

ART UNIT

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/091,360	<b>Applicant(s)</b> TSIPOURAS ET AL.	
	<b>Examiner</b> Lori A. Clow, Ph.D.	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 11 February 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 40,41,45 and 47-53 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 40,41,45 and 47-53 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/21/08</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicants' response, filed 11 February 2008, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 40, 41, 45, and 47-53 are currently pending. Claims 1-39, 42-44 and 46 have been cancelled.

#### **Information Disclosure Statement**

The Information Disclosure Statement filed 21 May 2008 has been partially considered. References for AnueVysion and UroVysion have not been considered, as they lack a publication date. A signed copy of PTO form 1449 is included with this Office Action.

#### **Claim Objections**

Claims 45 and 47 are objected to because of the following informalities:

Claim 45, as amended, recites, "in accordance with method of claim 48". This is grammatically incorrect and should read, "in accordance with **the** method of claim 48". Appropriate correction is requested.

Claim 47, as amended, recites, "and digitally record and store x and y coordinates. This is grammatically inconsistent with the rest of the claim and should be amended to read, "digitally recording and storing x and y coordinates". Appropriate correction is required.

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**Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 40, 41, 45, and 47-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,169,816 (Ravkin; previously cited), in view of US 2004/0072364 (Tisone et al.; newly cited). This rejection is newly applied and is necessitated by claim amendment.

The instant claims are drawn to a method for rare cell bright field and bright field microscopic image detection and identification.

Ravkin teaches computer implemented imaging, using a combination of brightfield and fluorescence images of smears of fetal nucleated red blood cells (NRBCs) and other objects, such as red blood cells (RBCs) and white blood cells (WBCs) (abstract, column 11 lines 65-67 to column 2, line 1). The objects in the sample are stained with a fluorescent dye that selectively stains nuclei and a dye that selectively stains fetal hemoglobin in the cytoplasm of fetal NRBCs. These include two different illumination schemes, such that candidate regions of interest (blobs)

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are identified for further processing (column 1, lines 65-67 to column 2, lines 1-20). The invention is directed to an evaluation that includes enrichment of fetal NRBCs from maternal blood, positive identification of fetal NRBCs (signal one), and genetic analysis (signal two) (column 3, lines 30-33).

In regard to claims 47, steps (i) and (ii) and claim 48, Ravkin teaches that a set of features that identify fetal NRBCs are created to distinguish them from other types of cells. This is done by creating contrast in cells containing fetal hemoglobin and another type of contrast in cells having a nucleus. The slide is reacted with a reagent (antibody) to produce a signal (column 3, line 58-667 to column 4, lines 1-6). The images are processed (digitized; column 4, line 53) to provide derivative images that are correlated to a region of interest. From there further analysis of only the region of interest is performed, such that the image falls into a specific class of object (column 7, lines 44-57). Ravkin teaches that the invention is carried out to identify objects for further analysis such as FISH. A FISH sample is prepared using probe that binds to a particular DNA sequence in the chromosomes in the sample and the probe is labeled. Slides are laid out with coordinates of reference points (column 4, lines 8-11). The system also comprises motor and lamp controllers (column 5, lines 11-25).

In regard to claim 48, Ravkin further teaches that the microscopic system is computerized (column 5, line 66-67 to column 7, lines 1-5). Further, the computer system comprises processors that are linked with any number of peripheral devices (column 6, lines 1-7).

In regard to claim 40, Ravkin teaches large field sample images (column 7, sections 5 and 6)

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Ravkin teaches varying concentrations of rare cells as in claim 41 at column 3, lines 41-45.

In regard to claim 45, Ravkin teaches a computer readable storage medium for the system (column 6, lines 59-67).

Ravkin does not specifically teach the embodiments of claim 47, step (iii) and claim 48 that are drawn to the computer-controlled dispensing system to apply the label or tag to the candidate image. However, Tisone et al. teach a dispensing apparatus and method for dispensing reagent onto a substrate in which the dispensing apparatus has a dispensing head that is responsive to a first signal to dispense droplets of reagent onto a substrate. The substrate or dispensing head are secured in association with a table or carriage. The table is responsive to a second signal for providing for relative X, X-Y or X-Y-Z motion. The controller is adapted to receive data representative of a desired reagent pattern and to output and coordinate the first and second signals so as to cause relative motion between the substrate and the dispensing head and to cause the dispensing head to dispense droplets of reagent at one or more desired locations (abstract). Tisone teach that the apparatus may be used for dispensing onto a glass slide (page 3, column 2, paragraph [0038]. In regard to claims 50, 51, and 53 the system moves in respect to the signals received and there are a series of stepper motors to move the platform, the dispensing head or carriage (page 4, column 4, paragraph [0048]. Tisone teaches that the system comprises displacement pumps for dispensing reagent (page 4, column 2, paragraph [0049] (as in claim 53).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have incorporated the reagent dispensing methods of Tisone with the computerized microscope rare cell detection system and methods of Ravkin, as Ravkin teaches

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that techniques for interfacing the computer to external instruments are known and the system may be in communication with a number of peripheral devices via a bus subsystem (column 6, lines 1-10). Further, Tisone motivates one to combine such methods, as well, as Tisone teaches that a host computer is the central controller (paragraph 0063) and that various configurations exist for the system (paragraph 0118 and 0119). One of ordinary skill in the art of computers could have clearly configured both such that the systems, when combined, meet the limitations of the instant claims.

Ravkin and Tisone do not teach the specific limitations of claims 48 and 52, however, it would have been obvious to one of skill in the art to dispense a label as the reagent, as the system uses fluorescent techniques. Further, it would have been obvious to have configured the system with the ability to move a slide to a thermocycling station for *in situ* hybridization, as Ravkin teaches FISH techniques.

### **Conclusion**

No claims are allowed.

The outstanding rejections under 35 USC 101, non-statutory subject matter are withdrawn in view of the claim amendments.

The outstanding rejections under 35 USC 112, 1<sup>st</sup> paragraph, enablement are withdrawn in view of the claim amendments.

The outstanding rejections under 35 USC 112, 2<sup>nd</sup> paragraph are withdrawn in view of the claim amendments.

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Applicant's arguments with regard to Ravkin are moot in view of the newly cited prior art rejection under 35 USC 103(a), as necessitated by claim amendment.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### **Inquiries**

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the



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USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

June 4, 2008

/Lori A. Clow, Ph.D./

Primary Examiner, Art Unit 1631